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10/777,010	02/11/2004	Carsten-Peter Carstens	25436/1344	3414

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EXAMINER
BURKHART, MICHAEL D

ART UNIT	PAPER NUMBER
1633	

NOTIFICATION DATE	DELIVERY MODE
04/18/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/777,010	CARSTENS, CARSTEN-PETER	
	Examiner	Art Unit	
	Michael Burkhart	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 December 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *45-61* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *45-61* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt and entry of the amendment dated 12/27/2007 is acknowledged. After entry of the amendment, claims 45-61 are pending and under examination.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Specification

The amendment filed 11/2/2006 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: SEQ ID NOs 14-16. **This objection is maintained for reasons made of record in the Office Action dated 9/27/2007, and for reasons set forth below.**

Response to Arguments

Applicant's arguments filed 12/27/2007 have been fully considered but they are not persuasive. Applicants essentially assert that: 1) pages 23-24 of the specification indicate that the claimed tRNA genes were isolated using PCR primers that anneal at specific base pairs in the GenBank sequences, thus providing an acceptable notation for known sequences that complies with the requirements of 35 USC 112; 2) the objection to the amendment for introducing new matter is form over substance, and is at odds with the decision of the Federal Circuit in *Falko-Gunter Falkner v. Inglis*; 3) the sequences were available from Genbank and other literature sources.

Regarding 1), this is not a 35 USC 112 rejection, although 35 USC 132(a) is based upon 35 USC 112. What is relevant is that there is no disclosure of SEQ ID NOs 14-16 in the disclosure as originally filed, for reasons set forth in the previous Office Action. Hence, the disclosure comprises New Matter.

Regarding 2) and 3), the case law cited, *Falko-Gunter Falkner v. Inglis,* is not on point. In *Falkner v. Inglis*, the claims were generic, and not directed to a specific poxvirus sequence. In the case of *Falkner v. Inglis*, applicants would have been required to bring in every poxvirus sequence because the claims were generic, not directed to a specific sequence. For example, the claims at issue in *Falkner v. Inglis* were claim 1 from Falkner et al (5,770,212):

1. A vaccine comprising

(a) a defective poxvirus that lacks a function imparted by an essential region of its parental poxvirus, wherein

(i) said defective poxvirus comprises a DNA polynucleotide encoding an antigen and said DNA polynucleotide is under transcriptional control of a promoter, and (ii) the function can be complemented by a complementing source;
and

(b) a pharmaceutically acceptable carrier.;

and claim 29 from Inglis:

A vaccine comprising a pharmaceutically acceptable excipient and an effective immunizing amount of a mutant virus, wherein said mutant virus is a mutant *poxvirus* and has a genome which has an inactivating mutation in a viral gene, said viral gene being essential for the production of infectious new virus particles, wherein said mutant virus is able to cause production of infectious new virus particles in a complementing host cell gene expressing a gene which complements said essential viral gene, but is unable to cause production of infectious new virus particles when said mutant virus infects a host cell other than a complementing host cell; for prophylactic or therapeutic use in generating an immune response in a subject.

That is not the case here, as the claims recite specific sequences, hence, such sequences are essential, claimed subject matter and must be in the specification. In *Falkner v. Inglis* the

Federal Circuit indicates that the relevant poxvirus sequences were nonessential subject matter, acknowledging that nonessential subject matter need not be incorporated by reference:

> [14] Here, the patentee did not attempt incorporation by reference. Where, of course, certain material that is not present in the specification is deemed nonessential to the satisfaction of the written description requirement, the issue of proper incorporation by reference *vel non* is irrelevant.

Thus, the decision in *Falkner v. Inglis* is silent regarding the incorporation by reference, or direct recitation, of essential, claimed subject matter, and cannot serve to provide a basis for adding new matter to the specification, as found in the instant application.

Finally, it is noted that there is no proper incorporation by reference of the Genbank Accession numbers, i.e., the root words "incorporate" and/or "reference" have been omitted. See 37 CFR 1.57(b)(1).

Claim Rejections - 35 USC § 112

Claims 50-52 and 59-61 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This rejection is maintained for reasons made of record in the Office Action dated 9/27/2007, and for reasons set forth below.**

Response to Arguments

Applicant's arguments filed 12/27/2007 have been fully considered but they are not persuasive. Applicants essentially assert that: 1) there is no per se rule that written description must be satisfied by recitation of the actual sequence, and make reference to the arguments above from *Falkner v. Inglis*; 2) the *Enzo v. Gen-Probe* decision provides more support for the findings in *Falkner v. Inglis*; 3) for these reasons, applicants are not required to recite or incorporate by reference the nucleotide sequences.

Regarding 1) and 3), the case law cited, *Falko-Gunter Falkner v. Inglis,* is not on point. In *Falkner v. Inglis*, the claims were generic, and not directed to a specific poxvirus sequence. In the case of *Falkner v. Inglis*, applicants would have been required to bring in every poxvirus sequence because the claims were generic, not directed to a specific sequence. See the reproduction of the claims at issue in *Falkner v. Inglis* above. That is not the case here, as the claims recite specific sequences, hence, such sequences are essential, claimed subject matter and must be in the specification. In *Falkner v. Inglis* the Federal Circuit indicates that the relevant poxvirus sequences were nonessential subject matter, acknowledging that nonessential subject matter need not be incorporated by reference (see above). Thus, the decision in *Falkner v. Inglis* is silent regarding the incorporation by reference, or direct recitation, of essential, claimed subject matter, and cannot serve to provide a basis for adding new matter to the specification, as found in the instant application.

Regarding 2) and 3), the case law cited, *Enzo v. Gen-Probe*, is not on point. In the case of *Enzo*, the nucleotide sequences were claimed as inserts in cell lines deposited with the ATCC, an acceptable depository under the biological deposit requirements (see 37 CFR 1.801-1.809). That is not the case here, as there is no evidence that applicants have deposited the claimed

nucleotide sequences. GenBank Accession numbers are not considered such a deposit for reasons set forth in the previous Office Action, and for the reasons set forth in 37 CFR 1.803. Further, it is noted that in the paragraph cited by applicants, *Enzo* incorporated the deposits by reference. It is noted that in the instant application, there is no proper incorporation by reference of the Genbank Accession numbers, i.e., the root words "incorporate" and/or "reference" have been omitted. See 37 CFR 1.57(b)(1).

Claim Rejections - 35 USC § 103

Claims 45-48, 53-56, and 58 are rejected under 35 U.S.C. 103(a) as being unpatentable over Del Tito et al (cited in the IDS of 2/11/2004) in view of Nakamura et al, Zhang et al, Saier, Kawakami et al, Clouthier et al (see applicants' exhibits A-G in the response filed 9/26/2002 in parent application 09/492,590) and Sprinzl et al (Nuc. Acids Res., 1998). **This rejection is maintained for reasons made of record in the Office Action dated 9/27/2007, and for reasons set forth below.**

Response to Arguments

Applicant's arguments filed 12/27/2007 have been fully considered but they are not persuasive. Applicants essentially assert that: 1) the teachings of the references do not teach all the limitations of the claims; 2) Del Tito et al teaches away from the claimed invention; 3) the invention has met with commercial success, as set forth in the Rule 132 declarations submitted as Attachments D and E

Regarding 1), applicants fail to point out what limitation(s) are not taught by the prior art cited above.

Regarding 2), this assertion is based on a single example from Del Tito et al, (ileX and argU were not as effective as ileX alone), and general teachings from other prior art references (e.g. Rojiani et al, Sharp et al) that overexspression of tRNA genes can be deleterious to the cell. However, as set forth in the previous Office Action, Del Tito et al provide another example (Mup^r IRS) wherein the combination of ileX and argU was more effective than ileX alone (Table 2). Furthermore, Del Tito et al present a solution to such problems: "…problems in expression can be avoided by a careful inspection of the coding sequence and inclusion of appropriate tRNA genes or necessary site-specific mutations." (page 7087, first column). Thus, the totality of the prior art does not support a conclusion that the references teach away from the claimed invention. Any vague problems taught by Rojiani et al Sharp et al are addressed by the results and teachings of Del Tito et al.

Regarding 3), with regard to the Rule 132 Declarations provided by Mary Buchanan, the declarations have been considered but are not deemed persuasive with regard to obviousness of the claimed invention. There is no background provided against which to judge the degree of success for the claimed invention. Are there any other host strains on the market today for expression of polypeptides comprising rarely used codons? How do the sales figures for the embodiments described by Ms. Buchanan compare to such strains? How do the sales figures compare to other expression hosts available on the market? Gross sales figures alone do not show commercial success absent any evidence to market share, the time period during which the product was sold the claimed invention is not obvious. Some relevant background figure needs to be provided against which the figures provided in the declaration can be compared.

There remains no meaningful background against which the sales figures presented can be weighed to determine if the demonstrated sales are so indicative of commercial success as to make the claimed invention unobvious.

As indicated above, the evidence of record does not indicate that the level of commercial sales of a few specific embodiments of the claimed invention is necessarily due to some aspect of the claimed invention. Without the appropriate background against which to judge (e.g. a commercially available vector comprising the tRNA genes taught by Del Tito et al), it is impossible to make the judgment that there is some aspect of applicants' invention that contributes to significant commercial success or that the demonstrated sales are of such a magnitude as to make the claimed invention unobvious over the prior art.

As was demonstrated in making the rejection, the basic concept of supplying different rarely used tRNA genes in a cell to maximize expression of a desired gene product was clearly known at the time of filing and the raw materials (i.e. rare tRNA genes and rarely-used codons) were readily available in the art at the time of filing. The authors of the base reference, Del Tito et al, teach that "...problems in expression can be avoided by a careful inspection of the coding sequence and inclusion of appropriate tRNA genes or necessary site-specific mutations." Del Tito et al conclude that the coexpression of minor tRNAs such as ileX or argU can be utilized to overcome translational stresses due to the presence of rarely used codons within the coding sequence for a gene of interest (page 7091, column 1, paragraph 3). The claimed invention differs from the teachings of Del Tito et al only in the exact tRNA genes, and/or, in the number of tRNA genes that are comprised within the DNA constructs of the invention.

Claims 49 and 57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Del Tito et al, Nakamura et al, Zhang et al, Saier, Kawakami et al, Clouthier et al, and Sprinzl et al as applied to claims 45-48, 53-56, and 58 above, and further in view of Skerra et al (U.S. 5,849,576, 1998). **This rejection is maintained for reasons made of record in the Office Action dated 9/27/2007, and for reasons set forth below.**

Response to Arguments

Applicant's arguments filed 12/27/2007 have been fully considered but they are not persuasive. Applicants essentially assert that: 1) the teachings of the references do not teach all the limitations of the claims; 2) Skerra et al does not remedy the deficiencies of Del Tito, Nakamura, Zhang, Saier, Kawakami, Clouthier, and Sprinzl et al above.

Regarding 1), applicants fail to point out what limitation(s) are not taught by the prior art cited above.

Regarding 2), Del Tito, Nakamura, Zhang, Saier, Kawakami, Clouthier, and Sprinzl et al are not considered to have any deficiencies, for reasons et forth above.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Burkhart whose telephone number is (571)272-2915. The examiner can normally be reached on M-F 8AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Michael Burkhart
Art Unit 1633

/Michael Burkhart/
Primary Examiner, Art Unit 1633